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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/724,274	RAMAKRISHNAN ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/26/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-78* is/are pending in the application.

4a) Of the above claim(s) *64-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 51-78 are all the pending claims for this application.

2. Claims 64-78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim.

3. Claims 51-63 are all the pending claims under examination for this application. The Examiner has withdrawn the species restriction for the heavy chain variable and light chain variable sequences, thus SEQ ID NOs: 1, 25, 28 and 31, and 7, 26 and 32, respectively, are all the sequences under examination.

4. Applicant's arguments filed in the Response of 10/20/06 have been fully considered but they are not persuasive in overcoming all of the rejections as set forth below.

Applicant's amendments

5. Applicant's correction of the cross-referencing to related applications in the specification to properly identify the provisional application, 60/508,149, filed on 12/30/03 has been considered and entered.

6. Applicants submission of a corrected drawing for Figure 3 labeling each of the sequences with SEQ ID NOs: 46 and 47 has been considered and entered.

7. The revised Sequence Listing, CRF and statement have been considered and entered. Applicants' explanation of the amendments to the revised Sequence Listing on

p. 9, ¶8- p. 10, ¶1 of the Response of 10/26/06 is acknowledged as not raising any issue of new matter.

8. The amendment of Claims 51 and 55-59 in view of the restriction/election of sequences has been considered and entered.

Objections Withdrawn

Specification

9. The objection to disclosure for containing an embedded hyperlink and/or other form of browser-executable code on page 14, line 20, page 15, line 26, and page 44, line 10 is withdrawn in view of the amended specification, and further in view of Applicants comments on p. 10, ¶6 of the Response of 10/26/06.

10. The objection to the Brief Description of the Drawings for Figure 2 on page 8 listing SEQ ID NOs: 1-12 is withdrawn in view of the amendment of the figure legend to indicating that the sequences correspond to Figure 1, and further in view of Applicants comments on p. 10, ¶7 of the Response of 10/26/06.

Rejections Withdrawn

Claim Rejections - 35 USC § 112, second paragraph

11. The rejection of Claim 51 for lacking antecedent basis in reciting the limitation "the constant region" in line 8 is withdrawn in view of the amendment of the claims to recite "a constant region", and further in view of Applicants comments on p. 10, ¶8 of the Response of 10/26/06.

12. The rejection of Claims 51 and 55 as to the uncertainty of the requirement for both the heavy chain variable region and the light chain variable region for the chimeric or humanized anti-alpha5beta1 antibody is withdrawn in view of Applicants comments on p. 11, ¶1 of the Response of 10/26/06.

Rejections Maintained

35 USC § 112, first paragraph: written description

13. The rejection of Claims 51-58 and 63 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is maintained.

Applicant's arguments filed in the Response of 10/26/06 on p. 11, ¶2- p.12, ¶4 have been fully considered but they are not persuasive. Applicants allege that "five other distinct humanized versions of the IIA1 VH and VL (SEQ ID NOs: 2-6 and 8-12)" are disclosed, and "as shown in Figure 2 VH1.0 (SEQ ID NO: 2) includes substitutions at 17 amino acids of the total of 124 positions relative to SEQ ID NO: 1" in addition to SEQ ID NOs: 31 and 32. "For example, written support for variants of HUM200 (SEQ ID NOs: 31 and 32) with less than 100% sequence identity may be found in SEQ ID NOs: 1-6 and 7-12, respectively".

The Examiner submits that Applicants explanation of the written support for the species of VH and VL embodiments is confusing and contradictory. For example, on p. 11, ¶3 at lines 8-10, they state that SEQ ID NOs: 31 and 32 are variants of SEQ ID NOs: 1 and 7, respectively. Then on p. 12, ¶2, they state that SEQ ID NOs: 1 and 7 are

variants of SEQ ID NOs: 31 and 32 having less than 100% identity, respectively. On this basis alone, it is not clear which sequences are variants of which.

Secondly, Applicants allege that SEQ ID NO:2 is a representative example of a sequence having less than 100% identity with its corresponding parent SEQ ID NO:1. A simple calculation of the number of substitutions (17) per total number of amino acid residues for the sequence (124) shows a difference of 13.7% (i.e., 86.3% identity). Then on p. 13, ¶2, Applicants state that the percent identity between SEQ ID NO:2 and SEQ ID NO:1 is 87%. Irrespective of these differences, the example does not even meet the claim limitation for a sequence "having at least 95% identity".

Thirdly, Applicants have not provided or cited any examples of species where the amino acid sequence is at least 95% identical to SEQ ID NOs: 1, 7, 25, 26, 28 and 31 and 32. For example, do the sequences of SEQ ID NOs: 2-6 and 8-12 meet the claim limitation of having "at least 95% identity to any one of SEQ ID NOs: 1, 25, 28, and 31 as well as 7, 26, and 32?

Therefore, Applicants are not in possession of a genus of antibodies that have heavy chains and light chains that are at least 95% identical to SEQ ID NOs: 1, 25, 28, and 31 as well as 7, 26, and 32, respectively, and the rejection is maintained.

35 USC § 112, first paragraph: enablement

14. The rejection of Claims 51-63 under 35 U.S.C. §112, first paragraph, as being non-enabled for chimeric or humanized antibodies that have heavy and light chains a) with at least 95% sequence identity to SEQ ID NOs: 1, 16, 20, 25, 28, and 31, as well

as 7, 18, 22, 26, and 32, respectively (Claims 51-58 and 63); or b) "comprising" SEQ ID NOs: 1, 16, 20, 25, 28, and 31, as well as 7, 18, 22, 26, and 32, respectively (Claims 59-63).

Applicant's arguments filed on p. 12, ¶6- p. 14, ¶2 have been fully considered but they are not persuasive. Applicants essentially reiterate the same arguments presented under the written description rejection discussed supra.

The Examiner submits that chimeric or humanized antibodies with VH and VL consisting of any one of SEQ ID NOs: 1, 16, 20, 25, 28, and 31, as well as 7, 18, 22, 26, and 32, respectively, are fully enabled for binding to $\alpha 5\beta 1$ integrin. But where, as in the instant case, the claims are directed to an infinite genus of anti-$\alpha 5\beta 1$ integrin antibodies, under MPEP 2164.02 ("Working Examples and a Claimed Genus"), when the claimed genus as a whole cannot be practiced without undue experimentation, then proof of enablement will be required for members of the claimed genus. And under MPEP 716.01(c), arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d. 600, 602, 145 USPQ 716, 718 (CCPA 1965).

The Examiner makes further note of the functional limitation of Claims 55-58 and 63, where the VH and VL of the antibody not only must meet the requirement of having "at least 95% identity" with SEQ ID NOs: 1, 16, 20, 25, 28, and 31, as well as 7, 18, 22, 26, and 32, respectively, in order to bind $\alpha 5\beta 1$ integrin but must also be enabled for 'inhibiting angiogenesis stimulated by VEGF."

Finally, Applicants arguments that the antibodies include some variation in the CDR (e.g., a single amino acid change) (p. 14, ¶1) are not found persuasive for the

following reasons. Applicants have not identified any examples of an antibody having even a single CDR substitution that meet all of the claim limitations, i.e., binding to $\alpha 5\beta 1$ integrin and/or inhibiting VEGF-stimulated angiogenesis. Further, it is noted that the features upon which applicant relies (i.e.,single amino acid substitution of a CDR) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification (and Applicants' arguments) are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For all of the foregoing reasons, the enablement rejection is maintained.

Double Patenting

15. The provisional rejection of Claims 51 and 54-63 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/830,956 ("'956") is maintained.

Applicants submit that the withdrawal of Claims 1-8 from the '956 application renders the rejection moot (p. 14, ¶3), however these arguments are not persuasive. Applicants have not cancelled Claims 1-8 and the claims are still pending in the co-pending application.

16. The rejection of Claims 51 and 54-63 as not being patentably distinct from claims 1-8 of commonly assigned 10/830,956 is maintained.

Applicants submit that the withdrawal of Claims 1-8 from the '956 application renders the rejection moot (p. 14, ¶3) however these arguments are not persuasive for the reasons set forth supra.

Conclusion

17. No claims are allowed.

18. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system; see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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